UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/840,795	04/23/2001	Erin E. Murphy	SF0818KQ	5250

28008 7590 11/30/2004

DNAX RESEARCH, INC.
LEGAL DEPARTMENT
901 CALIFORNIA AVENUE
PALO ALTO, CA 94304

EXAMINER	
O HARA, EILEEN B	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 11/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/840,795	MURPHY ET AL.	
	Examiner	Art Unit	
	Eileen O'Hara	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 September 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11-15,21 and 22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-15, 21 and 22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on Sept. 9, 2004 has been entered.

Claims Status

2. Claims 11-15, 21 and 22 are pending in the instant application. Claims 11 and 12 have been amended as requested by Applicant in the Paper filed Sept. 9, 2004.

All claims are currently under examination.

New Rejections

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

3, Claims 11-15, 21 and 22 are rejected under 35 U.S.C. 102(e) as being anticipated by Goddard et al., U.S. Patent No. 6,534,061, effective priority date April 12, 1999 (60/128,849).

Claims 11-15, 21 and 22 encompass binding compounds comprising an antibody binding site which specifically binds and is immunoreactive to at least 17 contiguous amino acids from the signal processed form of SEQ ID NOS: 15, 17 or 19, wherein the binding compound is an antibody molecule which may be a monoclonal or humanized antibody, present in a polyclonal antiserum, detectably labeled, sterile or in a buffered composition, and methods of using the binding compound to form a binding compound:antigen complex in a human biological sample.

Claims of Goddard et al. are drawn to an amino acid sequence (SEQ ID NO: 6) that is 99.5% identical to amino acids 1-205 of SEQ ID NO: 19 of the instant specification (one mismatch at amino acid 58), and comprises at least 17 contiguous amino acids of the signal processed form of SEQ ID NOS: 15 and 17. SEQ ID NO: 6 of Goddard et al. is identical to the first 47 and 58 amino acids of SEQ ID NOS: 15 and 17 of the instant application. Goddard et al. also teach antibodies to the protein, which may be a monoclonal or humanized antibody, present in a polyclonal antiserum, detectably labeled, sterile or in a buffered composition, and methods of using the binding compound to form a binding compound:antigen complex in a human biological sample (column 14, lines 8-21, column 36, lines 19-31, column 36, line 63 to column 41, line 38, and column 50, line 20 to column 51, line 14). Since the protein of Goddard et al. is identical to the protein of SEQ ID NO: 19 of the instant applications, the binding compounds of Goddard et al. anticipate the claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claim 15 is rejected under 35 U.S.C. 103(a) as being unpatentable over Goddard et al., U.S. Patent No. 6,534,061, and further in view of Akita et al., US Patent No. 5,968,511. Claim 15 encompasses the binding compound of claim 12 in a kit with instructions.

The teachings of Goddard et al. are described above. Goddard et al. does not teach the binding compounds in a kit with instructions.

Akita et al. teach a kit comprising antibody and instructions for use (claim 17).

It would have been *prima facie* obvious to the person of ordinary skill in the art at the time the invention was made to use antibody binding compounds of Goddard et al., and put them in a kit with instructions, as taught by Akita et al. The skilled artisan would be motivated to do so in order to use the antibody to detect protein in a biological or tissue sample in order to

determine where the protein was present, having the antibody in a kit would be convenient, and there would be a reasonable expectation of success, since antibody kits with instructions have been widely and successfully used in the field of biochemistry.

Maintained Rejections

Claim Rejections - 35 USC § 101 and § 112

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 11-15, 21 and 22 remain rejected under 35 U.S.C. §§ 101 and 112 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility, for reasons of record in the previous Office Action, Paper No. 8, at pages 4-7, Paper No. 13 at pages 3-8, the Paper mailed March 9, 2004 at pages 2-6, the Advisory Action mailed June 21, 2004, and below.

Applicants traverse the rejection and assert on pages 2-4 of the response that the instant application fulfills the utility requirement as set forth in 35 U.S.C. § 101 because the mRNA data provided in the specification and in the Declaration of Jeanine Mattson Pursuant to 37 C.F.R. § 1.132 demonstrates a specific and substantial utility. Applicants submit that the specification specifically identifies a utility in the regulation and development of lymphocytes, and diseases

associated with lymphocyte regulation and development, and discloses the expression of the mRNA in art-recognized models of lymphocyte mediated response/disease, *i.e.*, allergic lung response. Applicants submit that this specifically asserted utility is further supported by Dr. Mattson's declaration where data using quantitative PCR demonstrates the expression of RANK-like mRNA in a primate model from idiopathic pulmonary fibrosis, a lymphocyte mediated disease state. Applicants assert that the Examiner has provided no scientific rationale or even a specific comment to explain why the data provided in Dr. Mattson's Declaration is insufficient. Applicants further assert that one of ordinary skill in the art would find a specific and substantial utility in the data presented in the specification and Dr. Mattson's declaration, and provide the published paper of Li, in which the authors draw the identical conclusions regarding utility as the Applicants after applying the same technique used in Dr. Mattson's declaration. Applicants further submit that there is no requirement to provide evidence sufficient to establish that an asserted utility is true "beyond a reasonable doubt" or "as a matter of statistical certainty.", and Applicant is only required to provide evidence if, when considered as a whole, leads the skilled artisan to conclude that the asserted utility is more likely than not true.

Applicants' arguments have been fully considered but are not deemed persuasive. The declaration under 37 CFR 1.132 filed April 28, 2003 and resubmitted May 12, 2004 is insufficient to overcome the rejection of claims 11-15, 21 and 22 based upon lack of utility under 35 U.S.C. 101, and therefore the rejection under 102(e), as set forth in the previous Office actions because: although the data attached to the declaration demonstrate that the mRNA encoding the protein of SEQ ID NO: 17 is increased in a lung idiopathic pulmonary fibrosis model and in a lung macaque Ascaris challenge model, this does not provide information on the

activity or function of the protein, and does not supply a utility for the protein or antibody to the protein. Applicants' arguments that the specification specifically identifies a utility that is supported by the data and the declaration, in that the RANK-like protein (RANKL) is involved in the regulation and development of lymphocytes, and thus diseases associated with lymphocyte regulation and development, has been considered but not found persuasive. Although the RANKL receptor of the claimed invention has structural similarity to the TNF family of receptors, simply finding that its transcript is elevated in inflammation does not provide information on how the protein is actually functioning. Although it may be associated with inflammation somehow, there is no information how it is involved – causing inflammation, or resulting from inflammation, and it is not predictable what any activity the receptor has. The Li paper submitted as Exhibit B demonstrates that the Taqman analysis is a very sensitive method used to quantitate interleukin-1β upregulation in ischemia. However, the accuracy of the quantitation of the transcript is not the issue; the issue is that although up-regulated, how is the RANKL protein functioning. Additionally, Li analyzed a known inflammatory cytokine to see if it was involved in ischemic brain tolerance; Li did not determine that the interleukin-1β was an inflammatory cytokine based upon its up-regulation, and also states that though elevated, it may have a potential role in ischemic brain tolerance. Applicants arguments that a cytokine (receptor?) does not have to be expressed at a high level to definitively alter and influence the microenvironment or even the entire organ system in which it is expressed, has been considered but not found persuasive. Even if the receptor were up-regulated correspondingly with the transcript in these disease models, this does not provide one of ordinary skill in the art information on how the receptor is involved in these disease models, as discussed above.

Additionally, the proteins of SEQ ID NOS: 15, 17 and 19 are disclosed as being variant primate sequences of RANK-like protein, but are proteins that are of different lengths and have considerable differences in sequence, and appear to be splice variants. It would not be predictable that proteins so divergent would have the same activity. In the Declatation under 37 CFR 1.132 filed, Dr, Mattson states that real time PCR analysis was employed to quantify gene expression, using the sequence of SEQ ID NO:17 per manufacturer's instructions, in which the three C-terminal amino acids were not included in the SEQ ID NO. 17 used in the Taqman@ analysis. It is not predictable that the two other variants, SEQ ID NOS: 15 and 19, would also be up-regulated in lung inflammation.

Therefore, the rejections are maintained.

Claim Rejections - 35 USC § 102 and § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

6. Claims 11-14, 21 and 22 remain rejected under 35 U.S.C. 102(e) as being anticipated by Goddard et al., U.S. published application 20030092044, effective filing date April 12, 1999 (60/128,849), and claim 15 remains rejected under 35 U.S.C. 103(a) as being unpatentable over Goddard et al., U.S. published application 20030092044, and further in view of Akita et al., US Patent No. 5,968,511, for reasons of record in the previous Office Action, Paper No. 13, at pages 9-11, , the Paper mailed March 9, 2004 at pages 6-7.

Applicants submit that Goddard is not a proper reference under 35 U.S.C. 102(e) for reasons of record, and as Applicants have met their burden with regards to the utility requirement

for both the protein and the nucleic acid of RANK-like protein, Applicants maintain their traversal of the Examiner's refusal to properly award a priority date of at least Sept. 11, 1998.

Applicants' arguments have been fully considered but are not deemed persuasive. The nucleic acid sequences receive benefit under 35 USC § 119(e) to provisional application 60/099,999 because they are enabled for use under 35 USC § 112. However, the instant claims are directed to protein binding compounds of the expressed protein, and the protein is not enabled for use under 35 USC § 112 in the instant application or the provisional application for the reasons discussed above. Therefore binding compounds are not enabled for use under 35 USC § 112. The effective priority date of the claimed invention is the filing date of the parent 09/351,777, since the instant application is a continuation of 09/351,777. For these reasons, the rejections are maintained.

It is believed that all pertinent arguments have been answered.

Conclusion

7. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eileen B. O'Hara, whose telephone number is (571) 272-0878. The examiner can normally be reached on Monday through Friday from 10:00 AM to 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached at (571) 272-0961.

The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://portal.uspto.gov/external/portal/pair. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Eileen B. O'Hara, Ph.D.

Patent Examiner

EILEEN B. O'HARA
PATENT EXAMINER